Inducible cardiomyocyte-specific gene disruption directed by the rat Tnnt2 promoter in the mouse.

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Public Summary:
This article describes the development of a new genetic tool to study the development and disease of heart muscle.

Scientific Abstract:
We developed a conditional and inducible gene knockout methodology that allows effective gene deletion in mouse cardiomyocytes. This transgenic mouse line was generated by coinjection of two transgenes, a "reverse" tetracycline-controlled transactivator (rtTA) directed by a rat cardiac troponin T (Tnnt2) promoter and a Cre recombinase driven by a tetracycline-responsive promoter (TetO). Here, Tnnt2-rtTA activated TetO-Cre expression takes place in cardiomyocytes following doxycycline treatment. Using two different mouse Cre reporter lines, we demonstrated that expression of Cre recombinase was specifically and robustly induced in the cardiomyocytes of embryonic or adult hearts following doxycycline induction, thus, allowing cardiomyocyte-specific gene disruption and lineage tracing. We also showed that rtTA expression and doxycycline treatment did not compromise cardiac function. These features make the Tnnt2-rtTA;TetO-Cre transgenic line a valuable genetic tool for analysis of spatiotemporal gene function and cardiomyocyte lineage tracing during developmental and postnatal periods.